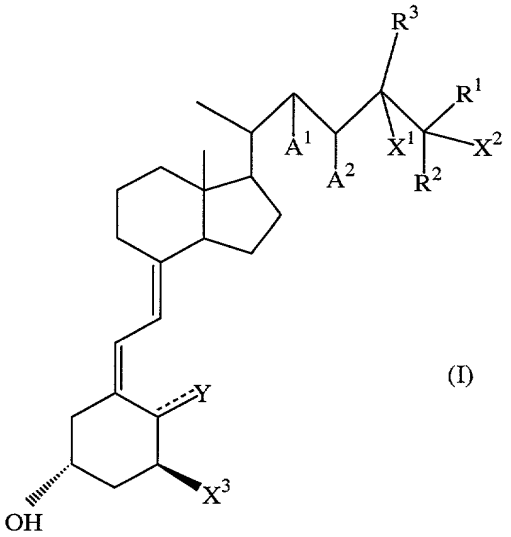
CLAIMS

1. A method of inhibiting hyperproliferation of malignant or neoplastic cells, comprising treating the cells episodically with an antiproliferative amount of an active vitamin D compound which is a hypocalcemic vitamin D compound having a hydrocarbon moiety at the C_{24} position, with reduced risk of hypercalcemia; the cells expressing a vitamin D receptor.

2. The method as claimed in claim 1 wherein the active vitamin D compound is a hypocalcemic vitamin D compound.

3. The method of claim 1, wherein the malignant cells are associated with cancers of the breast, colon, prostate, lung, neck and head, pancreas, endometrium, bladder, cervix, testes, ovaries, squamous cell carcinoma, myeloid and lymphocytic leukemia, lymphoma, medullary thyroid carcinoma, melanoma, multiple myeloma, retinoblastoma or sarcomas of the soft tissues and bone.

4. The method of claim 2, wherein the hypocalcemic vitamin D is a compound represented by formula (I):

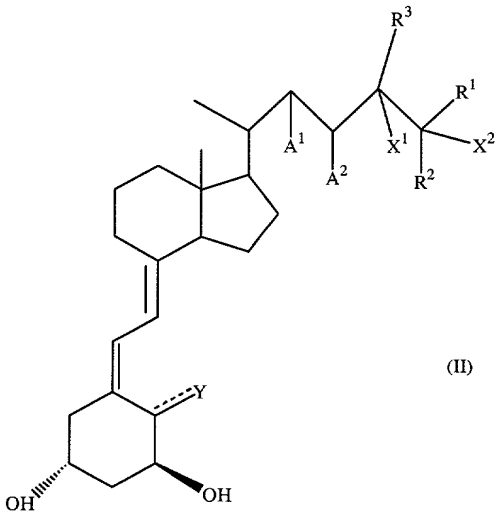


(I)

wherein A^1 and A^2 each are hydrogen or together represent a carbon-carbon bond, thus forming a double bond between C-22 and C-23; R^1 and R^2 are identical or different and are hydrogen, lower alkyl, lower fluoroalkyl, O-lower alkyl, lower alkenyl, lower fluoroalkenyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl, lower cycloalkyl with the

proviso that R^1 and R^2 cannot both be an alkenyl group, or taken together with the carbon to which they are bonded, form a C_3-C_8 cyclocarbon ring; R^3 is lower alkyl, lower alkenyl, lower fluoroalkyl, lower fluoroalkenyl, O-lower alkyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl or lower cycloalkyl; X^1 is hydrogen or hydroxyl, or, taken with R^3, constitutes a bond when R^3 is an alkenyl group, and X^2 is hydrogen or hydroxyl, or, taken with R^1 or R^2, constitutes a double bond, and X^3 is hydrogen or hydroxyl provided that at least one of X^1, X^2 and X^3 is hydroxyl; and Y is a methylene group if the bond to Y is a double bond or is a methyl group or hydrogen if the bond to Y is a single bond.

5. A method in accordance with claim 2 wherein the hypocalcemic vitamin D compound is a compound of formula (II):

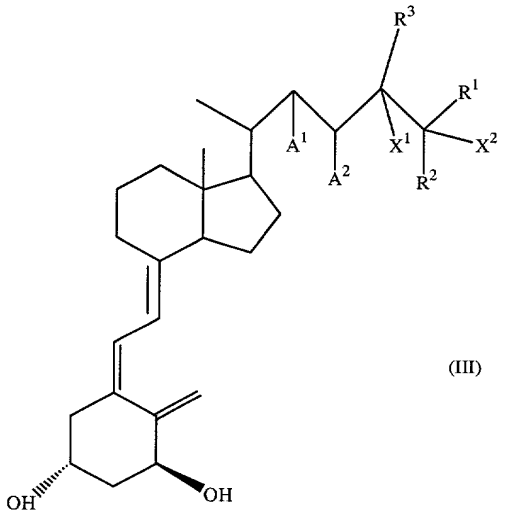


(II)

wherein A^1 and A^2 each are hydrogen or together represent a carbon-carbon bond, thus forming a double bond between C-22 and C-23; R^1 and R^2 are identical or different and are hydrogen, lower alkyl, lower fluoroalkyl, O-lower alkyl, lower alkenyl, lower fluoroalkenyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl, lower cycloalkyl with the proviso that R^1 and R^2 cannot both be an alkenyl group, or taken together with the carbon to which they are bonded, form a C_3-C_8 cyclocarbon ring; R^3 is lower alkyl, lower alkenyl, lower fluoroalkyl, lower fluoroalkenyl, O-lower alkyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl or lower cycloalkyl; X^1 is hydrogen or hydroxyl, or, taken with R^3, constitutes a bond when R^3 is an alkenyl group, and X^2 is hydrogen or hydroxyl, or,

taken with R^1 or R^2, constitutes a double bond, and Y is a methylene group if the bond to Y is a double bond or is a methyl group or hydrogen if the bond to Y is a single bond.

6. A method in accordance with claim 2, wherein the hypocalcemic vitamin D compound is a compound of formula (III):



(III)

wherein A^1 and A^2 each are hydrogen or together represent a carbon-carbon bond, thus forming a double bond between C-22 and C-23; R^1 and R^2 are identical or different and are hydrogen, lower alkyl, lower fluoroalkyl, O-lower alkyl, lower alkenyl, lower fluoroalkenyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl, lower cycloalkyl with the proviso that R^1 and R^2 cannot both be an alkenyl group, or taken together with the carbon to which they are bonded, form a C_3-C_8 cyclocarbon ring; R^3 is lower alkyl, lower alkenyl, lower fluoroalkyl, lower fluoroalkenyl, O-lower alkyl, O-lower alkenyl, O-lower acyl, O-aromatic acyl or lower cycloalkyl; X^1 is hydrogen or hydroxyl, or, taken with R^3, constitutes a bond when R^3 is an alkenyl group, and X^2 is hydrogen or hydroxyl, or, taken with R^1 or R^2, constitutes a double bond.

7. The method of claim 2 wherein the active vitamin D is 1α-hydroxyvitamin D_2 or 1α,24-dihydroxyvitamin D_2.

8. The method of claim 2 wherein the active vitamin D is 1α-hydroxyvitamin D_4; 1α,25-dihydroxyvitamin D_2; 1α,24,25-trihydroxyvitamin D_2 1α,25-dihydroxyvitamin D_4; 1α,24,25-trihydroxyvitamin D_4; 24-hydroxyvitamin D_2; or 24-hydroxyvitamin D_4.

9. The method as claimed in claim 2 wherein an amount of the active vitamin D compound is episodically administered to a human cancer patient, the amount being effective to inhibit the hyperproliferation of the neoplastic cells with reduced risk of hypercalcemia.

10. The method as claimed in claim 9 wherein the amount of active vitamin D is a high dose which is between about 10μg to about 200μg.

11. The method of claim 9 wherein the amount of the vitamin D compound is administered parenterally or orally in combination with a pharaceutically acceptable carrier.

12. The method of claim 11 wherein the amount of vitamin D compound is administered parenterally.

13. The method of claim 12 wherein the amount of vitamin D compound is administered intravenously.

14. The method of claim 9 wherein the amount administered is from about 10 μg to about 200 μg/dose given once per week to once every 12 weeks.

15. The method of claim 1 wherein the active vitamin D lacks a hydrocarbon moiety at the C-24 position.

16. The method of claim 15 wherein the active vitamin D is 1α,25-dihydroxyvitamin D_3 or 1α-dihydroxyvitamin D_3.

17. The method of claim 16 wherein the amount of the vitamin D compound is administered parenterally or orally in combination with a pharmaceutically acceptable carrier.

18. The method of claim 17 wherein the amount of vitamin D compound is administered parenterally.

19. The method of claim 18 wherein the amount of vitamin D compound is administered intravenously.

20. The method of claim 16 wherein the amount is administered is from about 10 μg to about 200 μg/dose given once per week to once every 12 weeks.

21. A method of inhibiting hyperproliferation of malignant or neoplastic cells, comprising treating the cells by co-administering an antihyperproliferative amount of an active vitamin D compound and an effective amount of an agent which is an antineoplastic agent, a bone agent, an antihypercalcemic agent or combinations thereof, the cells expressing a vitamin D receptor, the antiproliferative amount of the active vitamin D compound being administered on an episodic basis which is once per week to about once per 12 weeks.

22. The method of claim 21 wherein an amount of the active vitamin D compound and an amount of the agent are episodically co-administered to a human cancer patient, the amount of the active vitamin D effective to inhibit the hyperproliferation of the neoplastic cells.

23. The method of claim 22 wherein the agent is an antineoplastic agent.

24. The method of claim 23 wherein the antineoplastic agent is given episodically and the active vitamin D is given concurrently with the antineoplastic agent.

25. The method of claim 23 wherein the antineoplastic agent is an antimetabolite, an antimicrotubule agent, an alkylating agent, a platinum agent, an anthrocycline, a topisomerase inhibitor, an antibiotic, any other antineoplastic agent or combinations thereof.

26. The method of claim 22 wherein the agent is an antihypercalcemic agent.

27. The method of claim 26 wherein the antihypercalcemic agent is a bisphosphonate.

28. The method of claim 22 wherein an active vitamin D compound, an antineoplastic agent and an antihypercalcemic agent are co-administered.

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29. A method of inhibiting hyperproliferation of cells in a hyperproliferative disease, comprising treating the cells with an antihyperproliferative amount of an active D compound, the cells expressing a vitamin D receptor, the antiproliferative amount of the active vitamin D compound being administered on an episodic basis which is once per week to about once per 12 weeks.

30. The method of claim 29 wherein an amount of the active vitamin D compound is episodically administered to a human patient suffering from the hyperproliferative disease, the amount being effective to inhibit hyperproliferation of the cells.

31. The method of claim 30 wherein the amount is a high dose which is between about 10 μg and about 200 μg.

32. The method of claim 30 wherein the hyperproliferative disease is psoriasis.

33. A pharmaceutical therapy, comprising episodic co-administration of an active vitamin D compound with an antineoplastic agent.

34. A pharmaceutical combination, comprising:

a) an active vitamin D compound administered episodically;

b) an antineoplastic agent co-administered with the vitamin D compound.

35. A kit comprising:

a) an active vitamin D compound;

b) an agent which an antineoplastic agent, a bone agent, and antihypercalcemic agent or combinations thereof; and

c) instructions effective to perform the method of claim 22.

36. The kit of claim 35 wherein the agent is an antineoplastic agent.

37. The kit of claim 36 wherein the vitamin D compound and the antineoplastic agent are formulated for parenteral adminstration.

38. The kit of claim 36 wherein the vitamin D compound and the antineoplastic agent are manufactured physically separately and are intended for time-sequential co-administration.

39. The kit of claim 35 consisting essentially of

a) an active vitamin D compound;

b) an antineoplastic agent; and

c) instructions effective to perform the method of claim 22.

40. The kit of claim 35 consisting essentially of

a) an active vitamin D compound;

b) an antineoplastic agent;

c) an antihypercalcemic agent; and

d) instructions effective to perform the method of claim 22.

41. The kit of claim 35, wherein the active vitamin D compound is present in dosage of between about 10 μg and about 200 μg.